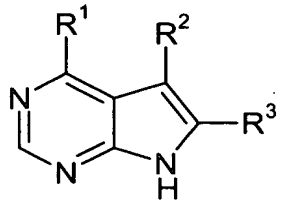
CLAIMS

1. A method of treating or preventing chronic organ transplant rejection in a mammal, including a human, comprising administering to said mammal an amount of a compound of the formula



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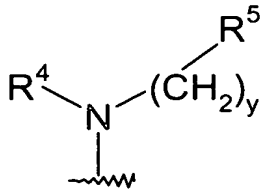
or the pharmaceutically acceptable salt thereof; wherein

R^1 is a group of the formula

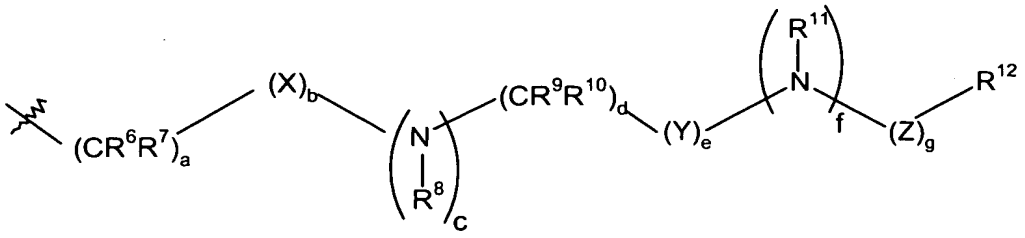


wherein y is 0, 1 or 2;

R^4 is selected from the group consisting of hydrogen, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylsulfonyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl wherein the alkyl, alkenyl and alkynyl groups are optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, $(C_1$-$C_4)$alkoxy, $(C_1$-$C_6)$acyloxy, $(C_1$-$C_6)$alkylamino, $((C_1$-$C_6)$alkyl$)_2$amino, cyano, nitro, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl or $(C_1$-$C_6)$acylamino; or R^4 is $(C_3$-$C_{10})$cycloalkyl wherein the cycloalkyl group is optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, $(C_1$-$C_6)$acyloxy, $(C_1$-$C_6)$acylamino, $(C_1$-$C_6)$alkylamino, $((C_1$-$C_6)$alkyl$)_2$amino, cyano, cyano$(C_1$-$C_6)$alkyl, trifluoromethyl$(C_1$-$C_6)$alkyl, nitro, nitro$(C_1$-$C_6)$alkyl or $(C_1$-$C_6)$acylamino;

R^5 is $(C_2$-$C_9)$heterocycloalkyl wherein the heterocycloalkyl groups must be substituted by one to five carboxy, cyano, amino, deuterium, hydroxy, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, halo, $(C_1$-$C_6)$acyl, $(C_1$-$C_6)$alkylamino, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy-CO-NH, $(C_1$-$C_6)$alkylamino-CO-, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$ alkynyl, $(C_1$-$C_6)$alkylamino, amino$(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$acyloxy$(C_1$-$C_6)$alkyl, nitro, cyano$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, nitro$(C_1$-$C_6)$alkyl, trifluoromethyl, trifluoromethyl$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$acylamino, $(C_1$-$C_6)$acylamino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$acylamino, amino$(C_1$-$C_6)$acyl, amino$(C_1$-$C_6)$acyl$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$acyl, $((C_1$-$C_6)$alkyl$)_2$amino$(C_1$-$C_6)$acyl, $R^{15}R^{16}$N-CO-O-, $R^{15}R^{16}$N-

CO-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-$S(O)_m$, $R^{15}R^{16}NS(O)_m$, $R^{15}R^{16}NS(O)_m$ $(C_1$-$C_6)$alkyl, $R^{15}S(O)_m R^{16}N$, $R^{15}S(O)_mR^{16}N(C_1$-$C_6)$alkyl wherein m is 0, 1 or 2 and R^{15} and R^{16} are each independently selected from hydrogen or $(C_1$-$C_6)$alkyl; or a group of the formula



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wherein a is 0, 1, 2, 3 or 4;

b, c, e, f and g are each independently 0 or 1;

d is 0, 1, 2, or 3;

X is $S(O)_n$ wherein n is 0, 1 or 2; oxygen, carbonyl or –C(=N-cyano)-;

Y is $S(O)_n$ wherein n is 0, 1 or 2; or carbonyl; and

Z is carbonyl, C(O)O-, C(O)NR- or $S(O)_n$ wherein n is 0, 1 or 2;

R^6, R^7, R^8, R^9, R^{10} and R^{11} are each independently selected from the group consisting of hydrogen or $(C_1$-$C_6)$alkyl optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, $(C_1$-$C_6)$acyloxy, $(C_1$-$C_6)$acylamino, $(C_1$-$C_6)$alkylamino, $((C_1$-$C_6)$alkyl$)_2$amino, cyano, cyano$(C_1$-$C_6)$alkyl, trifluoromethyl$(C_1$-$C_6)$alkyl, nitro, nitro$(C_1$-$C_6)$alkyl or $(C_1$-$C_6)$acylamino;

R^{12} is carboxy, cyano, amino, oxo, deuterium, hydroxy, trifluoromethyl, $(C_1$-$C_6)$alkyl, trifluoromethyl$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, halo, $(C_1$-$C_6)$acyl, $(C_1$-$C_6)$alkylamino, $((C_1$-$C_6)$alkyl$)_2$ amino, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy-CO-NH, $(C_1$-$C_6)$alkylamino-CO-, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$ alkynyl, $(C_1$-$C_6)$alkylamino, hydroxy$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$acyloxy$(C_1$-$C_6)$alkyl, nitro, cyano$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, nitro$(C_1$-$C_6)$alkyl, trifluoromethyl, trifluoromethyl$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$acylamino, $(C_1$-$C_6)$acylamino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$acylamino, amino$(C_1$-$C_6)$acyl, amino$(C_1$-$C_6)$acyl$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$acyl, $((C_1$-$C_6)$alkyl$)_2$amino$(C_1$-$C_6)$acyl, $R^{15}R^{16}N$-CO-O-, $R^{15}R^{16}N$-CO-$(C_1$-$C_6)$alkyl, $R^{15}C(O)NH$, $R^{15}OC(O)NH$, $R^{15}NHC(O)NH$, $(C_1$-$C_6)$alkyl-$S(O)_m$, $(C_1$-$C_6)$alkyl-$S(O)_m$-$(C_1$-$C_6)$alkyl, $R^{15}R^{16}NS(O)_m$, $R^{15}R^{16}NS(O)_m$ $(C_1$-$C_6)$alkyl, $R^{15}S(O)_m R^{16}N$, $R^{15}S(O)_mR^{16}N(C_1$-$C_6)$alkyl wherein m is 0, 1 or 2 and R^{15} and R^{16} are each independently selected from hydrogen or $(C_1$-$C_6)$alkyl;

R^2 and R^3 are each independently selected from the group consisting of hydrogen, deuterium, amino, halo, hydoxy, nitro, carboxy, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, trifluoromethyl, trifluoromethoxy, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, $(C_3$-$C_{10})$cycloalkyl wherein the alkyl, alkoxy or cycloalkyl groups are optionally substittued by one to three groups selected from halo, hydroxy, carboxy, amino $(C_1$-$C_6)$alkylthio, $(C_1$-$C_6)$alkylamino, $((C_1$-$C_6)$alkyl$)_2$amino, $(C_5$-$C_9)$heteroaryl, $(C_2$-$C_9)$heterocycloalkyl, $(C_3$-$C_9)$cycloalkyl or $(C_6$-$C_{10})$aryl; or R^2 and R^3 are each independently $(C_3$-$C_{10})$cycloalkyl, $(C_3$-$C_{10})$cycloalkoxy, $(C_1$-$C_6)$alkylamino, $((C_1$-$C_6)$alkyl$)_2$amino, $(C_6$-$C_{10})$arylamino, $(C_1$-$C_6)$alkylthio, $(C_6$-$C_{10})$arylthio, $(C_1$-$C_6)$alkylsulfinyl, $(C_6$-$C_{10})$arylsulfinyl, $(C_1$-$C_6)$alkylsulfonyl, $(C_6$-$C_{10})$arylsulfonyl, $(C_1$-$C_6)$acyl, $(C_1$-$C_6)$alkoxy-CO-NH-, $(C_1$-$C_6)$alkyamino-CO-, $(C_5$-$C_9)$heteroaryl, $(C_2$-$C_9)$heterocycloalkyl or $(C_6$-$C_{10})$aryl wherein the heteroaryl, heterocycloalkyl and aryl groups are optionally substituted by one to three halo, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-CO-NH-, $(C_1$-$C_6)$alkoxy-CO-NH-, $(C_1$-$C_6)$alkyl-CO-NH-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy-CO-NH-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy-CO-NH-$(C_1$-$C_6)$alkoxy, carboxy, carboxy$(C_1$-$C_6)$alkyl, carboxy$(C_1$-$C_6)$alkoxy, benzyloxycarbonyl$(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkoxycarbonyl$(C_1$-$C_6)$alkoxy, $(C_6$-$C_{10})$aryl, amino, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxycarbonylamino, $(C_6$-$C_{10})$aryl$(C_1$-$C_6)$alkoxycarbonylamino, $(C_1$-$C_6)$alkylamino, $((C_1$-$C_6)$alkyl$)_2$amino, $(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, $((C_1$-$C_6)$alkyl$)_2$amino$(C_1$-$C_6)$alkyl, hydroxy, $(C_1$-$C_6)$alkoxy, carboxy, carboxy$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxycarbonyl, $(C_1$-$C_6)$alkoxycarbonyl$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy-CO-NH-, $(C_1$-$C_6)$alkyl-CO-NH-, cyano, $(C_5$-$C_9)$heterocycloalkyl, amino-CO-NH-, $(C_1$-$C_6)$alkylamino-CO-NH-, $((C_1$-$C_6)$alkyl$)_2$amino-CO-NH-, $(C_6$-$C_{10})$arylamino-CO-NH-, $(C_5$-$C_9)$heteroarylamino-CO-NH-, $(C_1$-$C_6)$alkylamino-CO-NH-$(C_1$-$C_6)$alkyl, $((C_1$-$C_6)$alkyl$)_2$amino-CO-NH-$(C_1$-$C_6)$alkyl, $(C_6$-$C_{10})$arylamino-CO-NH-$(C_1$-$C_6)$alkyl, $(C_5$-$C_9)$heteroarylamino-CO-NH-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylsulfonyl, $(C_1$-$C_6)$alkylsulfonylamino, $(C_1$-$C_6)$alkylsulfonylamino$(C_1$-$C_6)$alkyl, $(C_6$-$C_{10})$arylsulfonyl, $(C_6$-$C_{10})$arylsulfonylamino, $(C_6$-$C_{10})$arylsulfonylamino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylsulfonylamino, $(C_1$-$C_6)$alkylsulfonylamino$(C_1$-$C_6)$alkyl, $(C_5$-$C_9)$heteroaryl or $(C_2$-$C_9)$heterocycloalkyl;

effective in treating such a condition.

2. A method according to claim 1, wherein a is 0; b is 1; X is carbonyl; c is 0; d is 0; e is 0; f is 0; and g is 0.

3. A method according to claim 1, wherein a is 0; b is 1; X is carbonyl; c is 0; d is 1; e is 0; f is 0, and g is 0.

4. A method according to claim 1, wherein a is 0; b is 1; X is carbonyl; c is 1; d is 0; e is 0; f is 0; and g is 0.

5. A method according to claim 1, wherein a is 0; b is 1; X is –C(=N=cyano)-; c is 1; d is 0; e is 0; f is 0; and g is 0.

6. A method according to claim 1, wherein a is 0; b is 0; c is 0; d is 0; e is 0; f is 0; g is 1; and Z is –C(O)-O-.

7. A method according to claim 1, wherein a is 0; b is 1; X is $S(O)_n$; n is 2; c is 0; d is 0; e is 0; f is 0; and g is 0.

8. A method according to claim 1, wherein a is 0; b is 1; X is $S(O)_n$; n is 2; c is 0; d is 2; e is 0; f is 1; g is 1; and Z is carbonyl.

9. A method according to claim 1, wherein a is 0; b is 1; X is $S(O)_n$; n is 2; c is 0; d is 2; e is 0; f is 1; and g is 0.

10. A method according to claim 1, wherein a is 0; b is 1; X is carbonyl; c is 1; d is 0; e is 1; Y is $S(O)_n$; n is 2; f is 0; and g is 0.

11. A method according to claim 1, wherein a is 0; b is 1; X is $S(O)_n$; n is 2; c is 1; d is 0; e is 0; f is 0; and g is 0.

12. A method according to claim 1, wherein R^{12} is cyano, trifluoromethyl, $(C_1\text{-}C_6)$alkyl, trifluoromethyl$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkylamino, $((C_1\text{-}C_6)\text{alkyl})_2$amino, $(C_2\text{-}C_6)$alkynyl, cyano$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkyl-$S(O)_m$ wherein m is 0, 1 or 2.

13. A method according to claim 1, wherein said compound is selected from the group consisting of:

Methyl-[4-methyl-1-(propane-1-sulfonyl)-piperidin-3-yl]-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amine;

4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidine-1-carboxylic acid methyl ester;

3,3,3-Trifluoro-1-{4-methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidin-1-yl}-propan-1-one;

4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidine-1-carboxylic acid dimethylamide;

({4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidine-1-carbonyl}-amino)-acetic acid ethyl ester;

3-{4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidin-1-yl}-3-oxo-propionitrile;

3,3,3-Trifluoro-1-{4-methyl-3-[methyl-(5-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidin-1-yl}-propan-1-one;

1-{4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidin-1-yl}-but-3-yn-1-one;

1-{3-[(5-Chloro-7H-pyrrolo[2,3-d]pyrimidin-4-yl)-methyl-amino]-4-methyl-piperidin-1-yl}-propan-1-one;

1-{3-[(5-Fluoro-7H-pyrrolo[2,3-d]pyrimidin-4-yl)-methyl-amino]-4-methyl-piperidin-1-yl}-propan-1-one;

N-cyano-4-methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-N'-propyl-piperidine-1-carboxamidine;

N-cyano-4,N',N'-Trimethyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidine-1-carboxamidine;

Methyl-[(3R,4R)-4-methyl-1-(propane-1-sulfonyl)-piperidin-3-yl]-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amine;

(3R,4R)-)-4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidine-1-carboxylic acid methyl ester;

3,3,3-Trifluoro-1-{(3R,4R)-4-methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidin-1-yl}-propan-1-one;

(3R,4R)-4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidine-1-carboxylic acid dimethylamide;

{(3R,4R)-4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidine-1-carbonyl}-amino)-acetic acid ethyl ester;

3-{(3R,4R)-4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidin-1-yl}-3-oxo-propionitrile;

3,3,3-Trifluoro-1-{(3R,4R)-4-methyl-3-[methyl-(5-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidin-1-yl}-propan-1-one;

1-{(3R,4R)-4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidin-1-yl}-but-3-yn-1-one;

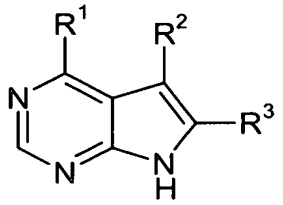
1-{(3R,4R)-3-[(5-Chloro-7H-pyrrolo[2,3-d]pyrimidin-4-yl)-methyl-amino]-4-methyl-piperidin-1-yl}-propan-1-one;

1-{(3R,4R)-3-[(5-Fluoro-7H-pyrrolo[2,3-d]pyrimidin-4-yl)-methyl-amino]-4-methyl-piperidin-1-yl}-propan-1-one;

(3R,4R)-N-cyano-4-methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-N'-propyl-piperidine-1-carboxamidine; and

(3R,4R)-N-cyano-4,N',N'-Trimethyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidine-1-carboxamidine.

14. A method of treating or preventing acute organ transplant rejection in a mammal, including a human, comprising administering to said mammal an amount of a compound of the formula



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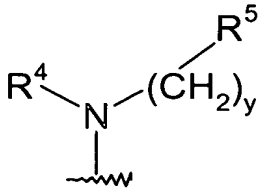
or the pharmaceutically acceptable salt thereof; wherein

R^1 is a group of the formula

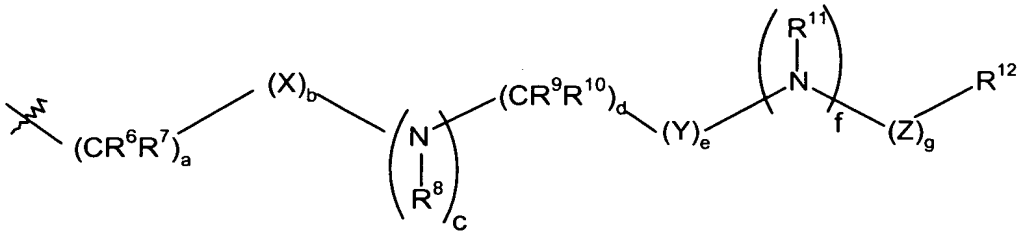


wherein y is 0, 1 or 2;

R^4 is selected from the group consisting of hydrogen, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylsulfonyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl wherein the alkyl, alkenyl and alkynyl groups are optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, $(C_1$-$C_4)$alkoxy, $(C_1$-$C_6)$acyloxy, $(C_1$-$C_6)$alkylamino, $((C_1$-$C_6)$alkyl$)_2$amino, cyano, nitro, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl or $(C_1$-$C_6)$acylamino; or R^4 is $(C_3$-$C_{10})$cycloalkyl wherein the cycloalkyl group is optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, $(C_1$-$C_6)$acyloxy, $(C_1$-$C_6)$acylamino, $(C_1$-$C_6)$alkylamino, $((C_1$-$C_6)$alkyl$)_2$amino, cyano, cyano$(C_1$-$C_6)$alkyl, trifluoromethyl$(C_1$-$C_6)$alkyl, nitro, nitro$(C_1$-$C_6)$alkyl or $(C_1$-$C_6)$acylamino;

R^5 is $(C_2$-$C_9)$heterocycloalkyl wherein the heterocycloalkyl groups must be substituted by one to five carboxy, cyano, amino, deuterium, hydroxy, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, halo, $(C_1$-$C_6)$acyl, $(C_1$-$C_6)$alkylamino, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy-CO-NH, $(C_1$-$C_6)$alkylamino-CO-, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$ alkynyl, $(C_1$-$C_6)$alkylamino, amino$(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$acyloxy$(C_1$-$C_6)$alkyl, nitro, cyano$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, nitro$(C_1$-$C_6)$alkyl, trifluoromethyl, trifluoromethyl$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$acylamino, $(C_1$-$C_6)$acylamino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$acylamino, amino$(C_1$-$C_6)$acyl, amino$(C_1$-$C_6)$acyl$(C_1$-$C_6)$alkyl, $(C_1$-

C_6)alkylamino(C_1-C_6)acyl, ((C_1-C_6)alkyl)$_2$amino(C_1-C_6)acyl, $R^{15}R^{16}$N-CO-O-, $R^{15}R^{16}$N-CO-(C_1-C_6)alkyl, (C_1-C_6)alkyl-S(O)$_m$, $R^{15}R^{16}$NS(O)$_m$, $R^{15}R^{16}$NS(O)$_m$ (C_1-C_6)alkyl, R^{15}S(O)$_m$ R^{16}N, R^{15}S(O)$_m$$R^{16}$N($C_1$-$C_6$)alkyl wherein m is 0, 1 or 2 and R^{15} and R^{16} are each independently selected from hydrogen or (C_1-C_6)alkyl; or a group of the formula



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wherein a is 0, 1, 2, 3 or 4;

b, c, e, f and g are each independently 0 or 1;

d is 0, 1, 2, or 3;

X is S(O)$_n$ wherein n is 0, 1 or 2; oxygen, carbonyl or –C(=N-cyano)-;

Y is S(O)$_n$ wherein n is 0, 1 or 2; or carbonyl; and

Z is carbonyl, C(O)O-, C(O)NR- or S(O)$_n$ wherein n is 0, 1 or 2;

R^6, R^7, R^8, R^9, R^{10} and R^{11} are each independently selected from the group consisting of hydrogen or (C_1-C_6)alkyl optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C_1-C_6)acyloxy, (C_1-C_6)acylamino, (C_1-C_6)alkylamino, ((C_1-C_6)alkyl)$_2$amino, cyano, cyano(C_1-C_6)alkyl, trifluoromethyl(C_1-C_6)alkyl, nitro, nitro(C_1-C_6)alkyl or (C_1-C_6)acylamino;

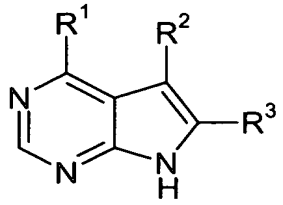
R^{12} is carboxy, cyano, amino, oxo, deuterium, hydroxy, trifluoromethyl, (C_1-C_6)alkyl, trifluoromethyl(C_1-C_6)alkyl, (C_1-C_6)alkoxy, halo, (C_1-C_6)acyl, (C_1-C_6)alkylamino, ((C_1-C_6)alkyl)$_2$ amino, amino(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-NH, (C_1-C_6)alkylamino-CO-, (C_2-C_6)alkenyl, (C_2-C_6) alkynyl, (C_1-C_6)alkylamino, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, (C_1-C_6)acyloxy(C_1-C_6)alkyl, nitro, cyano(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, nitro(C_1-C_6)alkyl, trifluoromethyl, trifluoromethyl(C_1-C_6)alkyl, (C_1-C_6)acylamino, (C_1-C_6)acylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)acylamino, amino(C_1-C_6)acyl, amino(C_1-C_6)acyl(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)acyl, ((C_1-C_6)alkyl)$_2$amino(C_1-C_6)acyl, $R^{15}R^{16}$N-CO-O-, $R^{15}R^{16}$N-CO-(C_1-C_6)alkyl, R^{15}C(O)NH, R^{15}OC(O)NH, R^{15}NHC(O)NH, (C_1-C_6)alkyl-S(O)$_m$, (C_1-C_6)alkyl-S(O)$_m$-(C_1-C_6)alkyl, $R^{15}R^{16}$NS(O)$_m$, $R^{15}R^{16}$NS(O)$_m$ (C_1-C_6)alkyl, R^{15}S(O)$_m$ R^{16}N,

$R^{15}S(O)_mR^{16}N(C_1\text{-}C_6)$alkyl wherein m is 0, 1 or 2 and R^{15} and R^{16} are each independently selected from hydrogen or $(C_1\text{-}C_6)$alkyl;

R^2 and R^3 are each independently selected from the group consisting of hydrogen, deuterium, amino, halo, hydoxy, nitro, carboxy, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, trifluoromethyl, trifluoromethoxy, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, $(C_3\text{-}C_{10})$cycloalkyl wherein the alkyl, alkoxy or cycloalkyl groups are optionally substittued by one to three groups selected from halo, hydroxy, carboxy, amino $(C_1\text{-}C_6)$alkylthio, $(C_1\text{-}C_6)$alkylamino, $((C_1\text{-}C_6)\text{alkyl})_2$amino, $(C_5\text{-}C_9)$heteroaryl, $(C_2\text{-}C_9)$heterocycloalkyl, $(C_3\text{-}C_9)$cycloalkyl or $(C_6\text{-}C_{10})$aryl; or R^2 and R^3 are each independently $(C_3\text{-}C_{10})$cycloalkyl, $(C_3\text{-}C_{10})$cycloalkoxy, $(C_1\text{-}C_6)$alkylamino, $((C_1\text{-}C_6)\text{alkyl})_2$amino, $(C_6\text{-}C_{10})$arylamino, $(C_1\text{-}C_6)$alkylthio, $(C_6\text{-}C_{10})$arylthio, $(C_1\text{-}C_6)$alkylsulfinyl, $(C_6\text{-}C_{10})$arylsulfinyl, $(C_1\text{-}C_6)$alkylsulfonyl, $(C_6\text{-}C_{10})$arylsulfonyl, $(C_1\text{-}C_6)$acyl, $(C_1\text{-}C_6)$alkoxy-CO-NH-, $(C_1\text{-}C_6)$alkyamino-CO-, $(C_5\text{-}C_9)$heteroaryl, $(C_2\text{-}C_9)$heterocycloalkyl or $(C_6\text{-}C_{10})$aryl wherein the heteroaryl, heterocycloalkyl and aryl groups are optionally substituted by one to three halo, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkyl-CO-NH-, $(C_1\text{-}C_6)$alkoxy-CO-NH-, $(C_1\text{-}C_6)$alkyl-CO-NH-$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy-CO-NH-$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy-CO-NH-$(C_1\text{-}C_6)$alkoxy, carboxy, carboxy$(C_1\text{-}C_6)$alkyl, carboxy$(C_1\text{-}C_6)$alkoxy, benzyloxycarbonyl$(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkoxycarbonyl$(C_1\text{-}C_6)$alkoxy, $(C_6\text{-}C_{10})$aryl, amino, amino$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxycarbonylamino, $(C_6\text{-}C_{10})$aryl$(C_1\text{-}C_6)$alkoxycarbonylamino, $(C_1\text{-}C_6)$alkylamino, $((C_1\text{-}C_6)\text{alkyl})_2$amino, $(C_1\text{-}C_6)$alkylamino$(C_1\text{-}C_6)$alkyl, $((C_1\text{-}C_6)\text{alkyl})_2$amino$(C_1\text{-}C_6)$alkyl, hydroxy, $(C_1\text{-}C_6)$alkoxy, carboxy, carboxy$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $(C_1\text{-}C_6)$alkoxycarbonyl$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy-CO-NH-, $(C_1\text{-}C_6)$alkyl-CO-NH-, cyano, $(C_5\text{-}C_9)$heterocycloalkyl, amino-CO-NH-, $(C_1\text{-}C_6)$alkylamino-CO-NH-, $((C_1\text{-}C_6)\text{alkyl})_2$amino-CO-NH-, $(C_6\text{-}C_{10})$arylamino-CO-NH-, $(C_5\text{-}C_9)$heteroarylamino-CO-NH-, $(C_1\text{-}C_6)$alkylamino-CO-NH-$(C_1\text{-}C_6)$alkyl, $((C_1\text{-}C_6)\text{alkyl})_2$amino-CO-NH-$(C_1\text{-}C_6)$alkyl, $(C_6\text{-}C_{10})$arylamino-CO-NH-$(C_1\text{-}C_6)$alkyl, $(C_5\text{-}C_9)$heteroarylamino-CO-NH-$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkylsulfonyl, $(C_1\text{-}C_6)$alkylsulfonylamino, $(C_1\text{-}C_6)$alkylsulfonylamino$(C_1\text{-}C_6)$alkyl, $(C_6\text{-}C_{10})$arylsulfonyl, $(C_6\text{-}C_{10})$arylsulfonylamino, $(C_6\text{-}C_{10})$arylsulfonylamino$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkylsulfonylamino, $(C_1\text{-}C_6)$alkylsulfonylamino$(C_1\text{-}C_6)$alkyl, $(C_5\text{-}C_9)$heteroaryl or $(C_2\text{-}C_9)$heterocycloalkyl;

effective in treating such a condition.

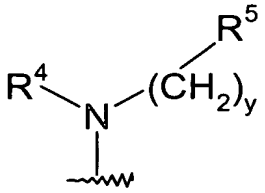
15. A pharmaceutical composition for treating or preventing chronic organ transplant rejection in a mammal, including a human, comprising an amount of a compound of the formula



I

or the pharmaceutically acceptable salt thereof; wherein

R^1 is a group of the formula

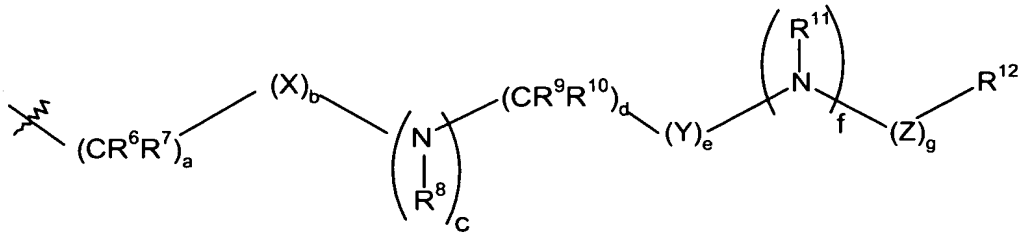


wherein y is 0, 1 or 2;

R^4 is selected from the group consisting of hydrogen, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylsulfonyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl wherein the alkyl, alkenyl and alkynyl groups are optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, $(C_1$-$C_4)$alkoxy, $(C_1$-$C_6)$acyloxy, $(C_1$-$C_6)$alkylamino, $((C_1$-$C_6)$alkyl$)_2$amino, cyano, nitro, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl or $(C_1$-$C_6)$acylamino; or R^4 is $(C_3$-$C_{10})$cycloalkyl wherein the cycloalkyl group is optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, $(C_1$-$C_6)$acyloxy, $(C_1$-$C_6)$acylamino, $(C_1$-$C_6)$alkylamino, $((C_1$-$C_6)$alkyl$)_2$amino, cyano, cyano$(C_1$-$C_6)$alkyl, trifluoromethyl$(C_1$-$C_6)$alkyl, nitro, nitro$(C_1$-$C_6)$alkyl or $(C_1$-$C_6)$acylamino;

R^5 is $(C_2$-$C_9)$heterocycloalkyl wherein the heterocycloalkyl groups must be substituted by one to five carboxy, cyano, amino, deuterium, hydroxy, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, halo, $(C_1$-$C_6)$acyl, $(C_1$-$C_6)$alkylamino, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy-CO-NH, $(C_1$-$C_6)$alkylamino-CO-, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$ alkynyl, $(C_1$-$C_6)$alkylamino, amino$(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$acyloxy$(C_1$-$C_6)$alkyl, nitro, cyano$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, nitro$(C_1$-$C_6)$alkyl, trifluoromethyl, trifluoromethyl$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$acylamino, $(C_1$-$C_6)$acylamino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$acylamino, amino$(C_1$-$C_6)$acyl, amino$(C_1$-$C_6)$acyl$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$acyl, $((C_1$-$C_6)$alkyl$)_2$amino$(C_1$-$C_6)$acyl, $R^{15}R^{16}$N-CO-O-, $R^{15}R^{16}$N-CO-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-S$(O)_m$, $R^{15}R^{16}$NS$(O)_m$, $R^{15}R^{16}$NS$(O)_m$ $(C_1$-$C_6)$alkyl,

$R^{15}S(O)_m R^{16}N$, $R^{15}S(O)_mR^{16}N(C_1\text{-}C_6)$alkyl wherein m is 0, 1 or 2 and R^{15} and R^{16} are each independently selected from hydrogen or $(C_1\text{-}C_6)$alkyl; or a group of the formula



II

wherein a is 0, 1, 2, 3 or 4;

b, c, e, f and g are each independently 0 or 1;

d is 0, 1, 2, or 3;

X is $S(O)_n$ wherein n is 0, 1 or 2; oxygen, carbonyl or –C(=N-cyano)-;

Y is $S(O)_n$ wherein n is 0, 1 or 2; or carbonyl; and

Z is carbonyl, C(O)O-, C(O)NR- or $S(O)_n$ wherein n is 0, 1 or 2;

R^6, R^7, R^8, R^9, R^{10} and R^{11} are each independently selected from the group consisting of hydrogen or $(C_1\text{-}C_6)$alkyl optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, $(C_1\text{-}C_6)$acyloxy, $(C_1\text{-}C_6)$acylamino, $(C_1\text{-}C_6)$alkylamino, $((C_1\text{-}C_6)\text{alkyl})_2$amino, cyano, cyano$(C_1\text{-}C_6)$alkyl, trifluoromethyl$(C_1\text{-}C_6)$alkyl, nitro, nitro$(C_1\text{-}C_6)$alkyl or $(C_1\text{-}C_6)$acylamino;

R^{12} is carboxy, cyano, amino, oxo, deuterium, hydroxy, trifluoromethyl, $(C_1\text{-}C_6)$alkyl, trifluoromethyl$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, halo, $(C_1\text{-}C_6)$acyl, $(C_1\text{-}C_6)$alkylamino, $((C_1\text{-}C_6)\text{alkyl})_2$ amino, amino$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy-CO-NH, $(C_1\text{-}C_6)$alkylamino-CO-, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$ alkynyl, $(C_1\text{-}C_6)$alkylamino, hydroxy$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$acyloxy$(C_1\text{-}C_6)$alkyl, nitro, cyano$(C_1\text{-}C_6)$alkyl, halo$(C_1\text{-}C_6)$alkyl, nitro$(C_1\text{-}C_6)$alkyl, trifluoromethyl, trifluoromethyl$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$acylamino, $(C_1\text{-}C_6)$acylamino$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$acylamino, amino$(C_1\text{-}C_6)$acyl, amino$(C_1\text{-}C_6)$acyl$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkylamino$(C_1\text{-}C_6)$acyl, $((C_1\text{-}C_6)\text{alkyl})_2$amino$(C_1\text{-}C_6)$acyl, $R^{15}R^{16}$N-CO-O-, $R^{15}R^{16}$N-CO-$(C_1\text{-}C_6)$alkyl, R^{15}C(O)NH, R^{15}OC(O)NH, R^{15}NHC(O)NH, $(C_1\text{-}C_6)$alkyl-$S(O)_m$, $(C_1\text{-}C_6)$alkyl-$S(O)_m$-$(C_1\text{-}C_6)$alkyl, $R^{15}R^{16}NS(O)_m$, $R^{15}R^{16}NS(O)_m$ $(C_1\text{-}C_6)$alkyl, $R^{15}S(O)_m$ $R^{16}N$, $R^{15}S(O)_mR^{16}N(C_1\text{-}C_6)$alkyl wherein m is 0, 1 or 2 and R^{15} and R^{16} are each independently selected from hydrogen or $(C_1\text{-}C_6)$alkyl;

R^2 and R^3 are each independently selected from the group consisting of hydrogen, deuterium, amino, halo, hydoxy, nitro, carboxy, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, trifluoromethyl, trifluoromethoxy, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, $(C_3$-$C_{10})$cycloalkyl wherein the alkyl, alkoxy or cycloalkyl groups are optionally substittued by one to three groups selected from halo, hydroxy, carboxy, amino $(C_1$-$C_6)$alkylthio, $(C_1$-$C_6)$alkylamino, $((C_1$-$C_6)$alkyl$)_2$amino, $(C_5$-$C_9)$heteroaryl, $(C_2$-$C_9)$heterocycloalkyl, $(C_3$-$C_9)$cycloalkyl or $(C_6$-$C_{10})$aryl; or R^2 and R^3 are each independently $(C_3$-$C_{10})$cycloalkyl, $(C_3$-$C_{10})$cycloalkoxy, $(C_1$-$C_6)$alkylamino, $((C_1$-$C_6)$alkyl$)_2$amino, $(C_6$-$C_{10})$arylamino, $(C_1$-$C_6)$alkylthio, $(C_6$-$C_{10})$arylthio, $(C_1$-$C_6)$alkylsulfinyl, $(C_6$-$C_{10})$arylsulfinyl, $(C_1$-$C_6)$alkylsulfonyl, $(C_6$-$C_{10})$arylsulfonyl, $(C_1$-$C_6)$acyl, $(C_1$-$C_6)$alkoxy-CO-NH-, $(C_1$-$C_6)$alkyamino-CO-, $(C_5$-$C_9)$heteroaryl, $(C_2$-$C_9)$heterocycloalkyl or $(C_6$-$C_{10})$aryl wherein the heteroaryl, heterocycloalkyl and aryl groups are optionally substituted by one to three halo, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-CO-NH-, $(C_1$-$C_6)$alkoxy-CO-NH-, $(C_1$-$C_6)$alkyl-CO-NH-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy-CO-NH-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy-CO-NH-$(C_1$-$C_6)$alkoxy, carboxy, carboxy$(C_1$-$C_6)$alkyl, carboxy$(C_1$-$C_6)$alkoxy, benzyloxycarbonyl$(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkoxycarbonyl$(C_1$-$C_6)$alkoxy, $(C_6$-$C_{10})$aryl, amino, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxycarbonylamino, $(C_6$-$C_{10})$aryl$(C_1$-$C_6)$alkoxycarbonylamino, $(C_1$-$C_6)$alkylamino, $((C_1$-$C_6)$alkyl$)_2$amino, $(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, $((C_1$-$C_6)$alkyl$)_2$amino$(C_1$-$C_6)$alkyl, hydroxy, $(C_1$-$C_6)$alkoxy, carboxy, carboxy$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxycarbonyl, $(C_1$-$C_6)$alkoxycarbonyl$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy-CO-NH-, $(C_1$-$C_6)$alkyl-CO-NH-, cyano, $(C_5$-$C_9)$heterocycloalkyl, amino-CO-NH-, $(C_1$-$C_6)$alkylamino-CO-NH-, $((C_1$-$C_6)$alkyl$)_2$amino-CO-NH-, $(C_6$-$C_{10})$arylamino-CO-NH-, $(C_5$-$C_9)$heteroarylamino-CO-NH-, $(C_1$-$C_6)$alkylamino-CO-NH-$(C_1$-$C_6)$alkyl, $((C_1$-$C_6)$alkyl$)_2$amino-CO-NH-$(C_1$-$C_6)$alkyl, $(C_6$-$C_{10})$arylamino-CO-NH-$(C_1$-$C_6)$alkyl, $(C_5$-$C_9)$heteroarylamino-CO-NH-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylsulfonyl, $(C_1$-$C_6)$alkylsulfonylamino, $(C_1$-$C_6)$alkylsulfonylamino$(C_1$-$C_6)$alkyl, $(C_6$-$C_{10})$arylsulfonyl, $(C_6$-$C_{10})$arylsulfonylamino, $(C_6$-$C_{10})$arylsulfonylamino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylsulfonylamino, $(C_1$-$C_6)$alkylsulfonylamino$(C_1$-$C_6)$alkyl, $(C_5$-$C_9)$heteroaryl or $(C_2$-$C_9)$heterocycloalkyl, effective in such disorders or conditions and a pharmaceutically acceptable carrier.